AD____ ____

(2)

THE ACUTE INHALATION TOXICITY OF PYROLYSIS PRODUCTS OF HALON 1301

ANNUAL REPORT

BRUCE E. LEHNERT
DOUGLAS M. STAVERT

DECEMBER 1, 1991

Supported by

U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
Fort Detrick, Frederick, Maryland 21702-5012

ARMY PROJECT ORDER NO. 87PP7032

Los Alamos National Laboratory
Los Alamos, New Mexico 87545

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	1 December 1991	Annual 1 Oct 90 - 30 Sep 91

4. TITLE AND SUBTITLE

The Acute Inhalation Toxicity of Pyrolysis Products of Halon 1301

5. FUNDING NUMBERS

87PP7832

62787A ✓
3M162787A875 AA
DA315677

6. AUTHOR(S)

Bruce E. Lehnert
Douglas M. Stavert

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Los Alamos National Laboratory
Los Alamos, New Mexico 87545

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research & Development Command
Fort Detrick
Frederick, Maryland 21702-5012

10. SPONSORING/MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION/AVAILABILITY STATEMENT

Approved for public release; distribution unlimited

12b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum 200 words)*

14. SUBJECT TERMS

RA 3; Toxicology; Gases; Acute Inhalation; Halon 1301; Pyrolysis Products

15. NUMBER OF PAGES

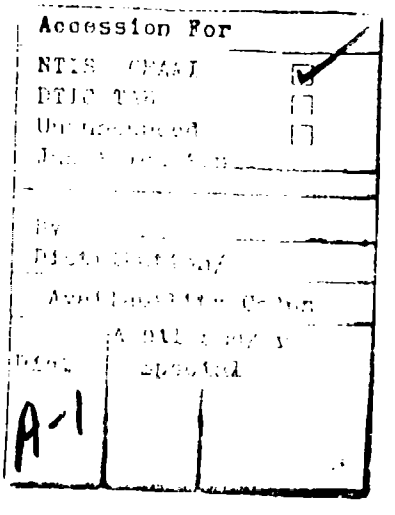
16 PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified		

FOREWORD

In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources Commission on Life Sciences, National Research Council (DHHS, PHS, NIH Publication No. 86-23, Revised 1985).

Citations of commercial organizations and trade names in this report do not constitute an official Department of the Army endorsement or approval of the products or services of these organizations.



SCIENTIFIC ACCOMPLISHMENTS/PROGRESS

Pathologic Responses to Inhaled Halide during Periods of Increased Minute Ventilation in Pseudo-Mouth Breathing and Nose-Breathing Rats

Gaseous halides can be generated as a pyrolysis products of the fire retardant Halon 1301, as well as from the combustion of other materials. Previous work in our laboratory (Toxicologist 10:A818, 1990; Fund. Appl. Toxicol. 16:636-655, 1991) has shown that the respiratory tract injury produced by the acute inhalation of relatively high mass concentrations of HCl, HF, and HBr (~1300 ppm) is localized within the nasal compartment during nose breathing (NB) and to the trachea and higher generation conducting airways during mouth breathing (MB) in the rat. For example, using lung gravimetric and histopathologic criteria, virtually no peripheral lung damage was observed in NB rats, and mild to no lung damage was observed in MB rats 24 hrs. after being exposed to 1300 ppm HCl for 30 min. It is presently unknown as to whether or not the lesions induced by acute high level inhalation of the halides can be extended more deeply into the lower respiratory tract by increases in minute ventilation (VE). The main objective of this study was to characterize the upper and lower respiratory tract lesions produced by inhaled halide in nose breathing and mouth breathing rats during CO_2 (5%) induced increased minute ventilation with the driving hypothesis being that the inhalation of halide during enhanced minute ventilation will increase the severity of resulting injury while also extending the injurious response to more peripheral regions of the respiratory tract. Inasmuch as we have previously demonstrated that HF, HBr, and HCl are essentially equivalent in producing toxic effects in the respiratory tract (Fund. Appl. Toxicol. 16:636-655, 1991) when inhaled at like concentrations (expressed in ppm), this task was undertaken using HCl as the model for all three of the halides.

Fischer-344 rats (SPF animals, preconditioned to partial body flow plethysmographs) were lightly anaesthetized uniformly with ethrane and either fitted with mouthpieces with attached silastic tracheal tubes (mouth breathers, MB), or they were allowed to awaken without further manipulation (nasal breathers, NB). After recovery, the NB and MB animals were placed into partial body plethysmographs and attached to an exposure chamber. The animals were provided clean filtered air for 5 min while pre-exposure ventilatory parameters were measured. Exposure atmospheres consisting of either filtered air with or without 5% CO_2 (controls), or 1000 ppm of HCl with or without 5% CO_2, were delivered to the rats for 20 min with the ventilatory parameters being measured over this exposure period. After cessation of the exposures, clean air was

delivered to the animals for 10 minutes while post-exposure ventilatory parameters were measured. After the exposures, the mouthpieces and tracheal tubes were removed from the MB animals. MB and NB animals were sacrificed 24 hrs. after the exposures for histologic analysis of their upper and lower respiratory tracts and for lung gravimetric measurements.

The mouthpieces were fabricated from the tips of polyethylene centrifuge tubes. The tracheal tube portion of each mouthpiece was made from soft silastic tubing, Figure 1. The device was placed intratracheally into a lightly anethetized rat using a modified otoscope, and it was secured into place via in cisor tooth grip holes drilled into the mouthpiece. A linear flow resistance of 0.11 cm H_2O/ml/sec was obtained with the device up to 20 ml/sec. The device had a deadspace volume of 0.3 ml. These values closely match the nasal resistance and deadspace values found for 250 gm Fischer rats (Journal of Aerosol Med. 1:51, 1988). After the device was in place, a nose clip was attached to the external nares, and a rubber band was placed over the mouth to prevent dislocation of the mouthpiece during exposure.

The HCl exposure atmospheres were generated by mixing pure HCl with anhydrous HEPA filtered air within a stainless steel mixing charnber. CO_2 was added and adjusted to 5% immediately upstream of the exposure chamber. Animals were exposed to the atmospheres while in a flow plethysmograph, Figure 2. A Teflon head piece with 2 rubber dams effectively sealed the body of the animal within the plethysmograph. A neck brace stabilized the animal during exposure.

Rat sacrifices were initiated by I.P injections of 50 mg pentobarbital sodium. The nasal cavity regions were prepared as described by Young (Fund. and Appl. Toxicol. 1:309-312, 1981), Figure 3. The trachea and lungs were excised, and the heart, extra-pulmonary mediastinal tissue, and the esophagus were removed. The lungs were blotted and weighed (Lung Wet Weight, LWW). The bronchus leading to the right cranial lobe (RCL) was ligated with fine suture, and the RCL was removed and weighed (Right Cranial Lobe Wet Weight, RCLWW). Following the gravimetric measurements, the trachea and lungs, minus the RCL, was cannulated with an 18-ga needle secured with ligature, and the lungs subsequently infused and fixed at a constant pressure of 30 cm H_2O with 10% formalin in phosphate buffered saline. The RCL were oven dried to a constant weight at 100°C for 36 hrs. and reweighed (Right Cranial Lobe Dry Weight, RCLDW).

Injury in the nasal cavity was graded according to severity and distribution. Endpoints of injury included epithelial necrosis, necrosis of lamina propria structures, the appearance of proteinaceous and cellular exudates, the infiltration of polymorphonuclear leukocytes (PMN) in the

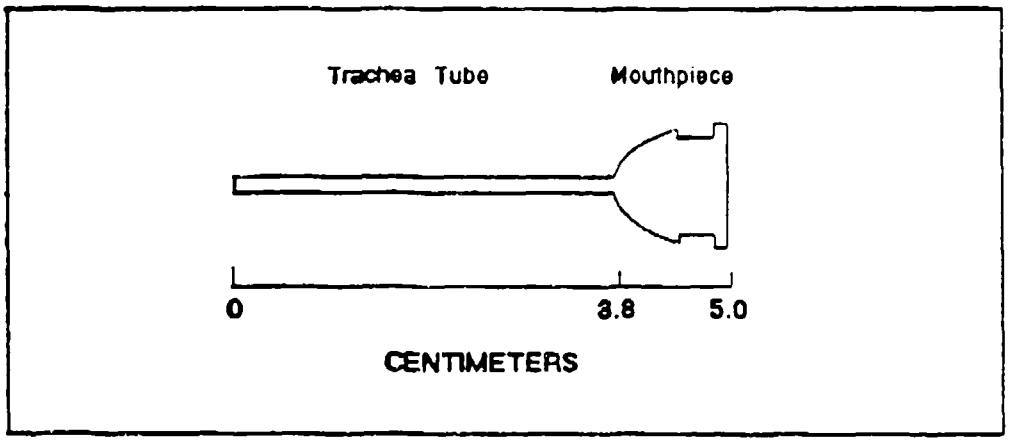


Figure 1. Mouthpiece used by mouth breathing rats.

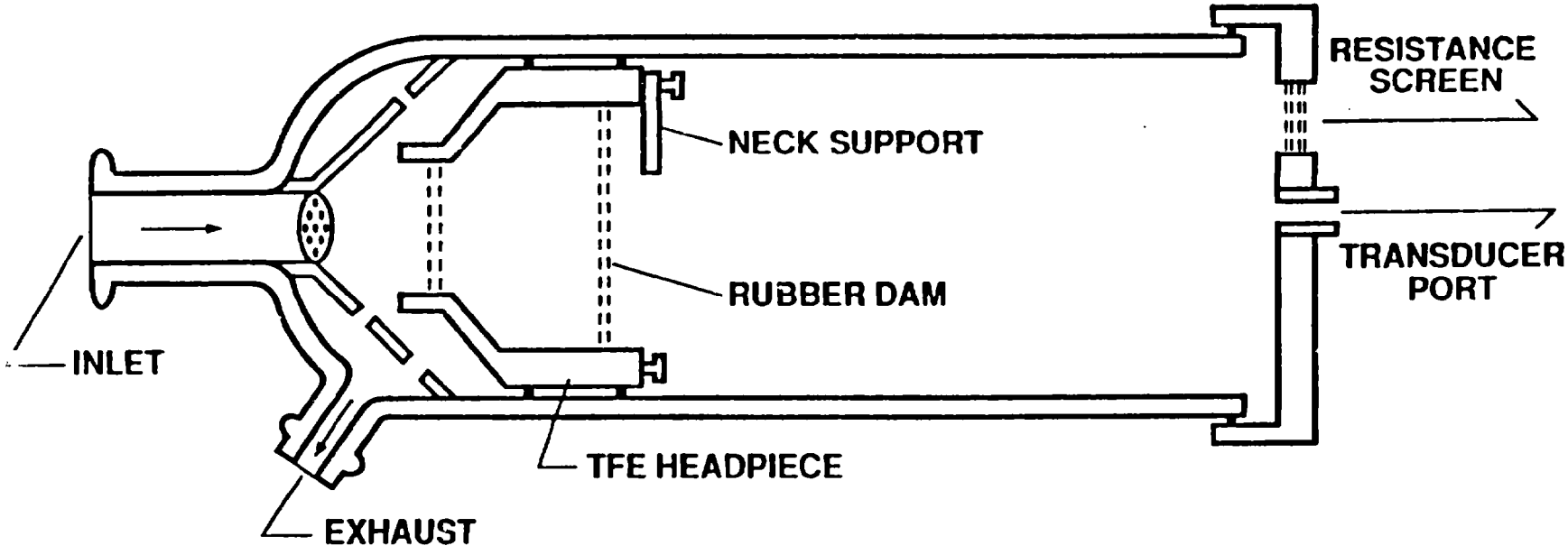


Figure 2. Partial body flow plethysmograph used for the halide exposure of mouth breathing and nose breathing rats. Rats were trained to sit within the plethysmograph during the 3 days prior to exposures.

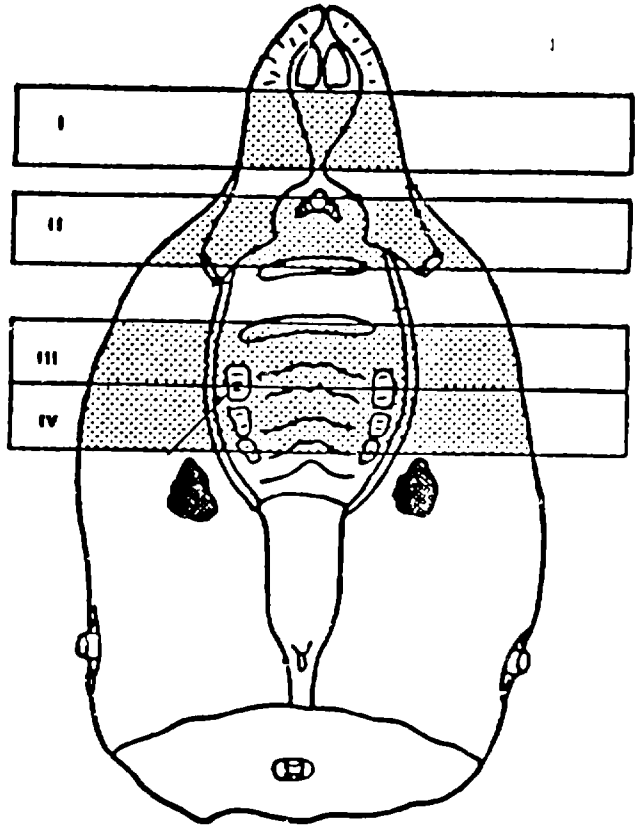


Figure 3. Nasal cavity regions prepared for histopathologic analysis. This figure was adapted from Young, Fund. Appl. Toxicol. 1:309-312, 1981.

epithelium and lamina propria, and hemorrhage into the lamina propria. A grading scale was used to quantitatively index the relative extent or distribution of an abnormality within a given tissue section. The distribution index for a given pathologic feature ranged from 1 to 4 with 1 = focal, 2 = few foci, 3 = moderate number of foci to many foci, and 4 = diffuse distribution. The severity index was used to describe the relative area affected, the amount of abnormal material present, and the relative numbers of cells abnormally occurring at affected sites. This index also ranged from 1 to 4 with 1 = small, 2 = moderate, 3 = large, and 4 = very large. Histopathologic assessments of the lung focused on the appearance of fibrin, accumulations of polymorphonucleated leukocytes (PMN) and excessive numbers of alveolar macrophages (AM), the extravasation of erythrocytes, vascular congestion, and alveolar cuboidal cell hyperplasia, i.e., Type II cell hyperplasia. With the exception of vascular congestion, a grading scale was used to quantitatively describe the relative severity of each of the above pathologic features in terms of their (1) distribution, i.e., relative number of terminal bronchioles showing a lesion in associated alveolar structures; (2) severity, or the relative number of periterminal bronchiolar alveolar structures affected; and (3) intensity, the relative amount of material or relative alterations of cells in the alveoli. The distribution index for a given pathologic feature ranged from 0 - 4 with 0 = not observed; 1 = single or focal in appearance; 2 = few but multifo cal; 3 = moderate number to many involved terminal airways; and 4 = all or essentially all alveolar structures were affected, i.e., diffuse. The relative severity index for a given pathologic feature ranged from 0 - 3 with 0 = no abnormality; 1 = the focal appearance of the abnormality in the periterminal alveolar structures; 3 = several affected alveolar structures; and 4 = many to all periterminal alveolar structures demonstrated the abnormality. The relative intensity index ranged from 0 to 4 with 0 = no abnormality, 1 = trace but detectable alterations in the amount of abnormal material, 2 = mild amount of small changes in cell numbers; 3 = moderate amount of abnormal material or abnormal number of cells, 4 = large amounts of intra-alveolar material of large changes in cell numbers.

NB rats increased VE approximately 70% during air + 5% CO_2 exposure, while the MB rats increased VE approximately 36% during the inhalation of air + 5% CO_2, Figure 4. NB rats decreased VE approximately 20% during 1000 ppm HCl inhalation. Concurrent HCl and 5% CO_2 inhalation by NB rats resulted in no increase in VE compared to the VE of HCl-only exposed NB rats, Figure 5. MB rats decreased their VE approximately 24% during HCl inhalation compared to air exposed MB rats, Figure 6. However, MB rats increased their VE approximately 45% during 5% CO_2 + HCl inhalation, when compared to MB inhalation of HCl alone. VE responses during air +

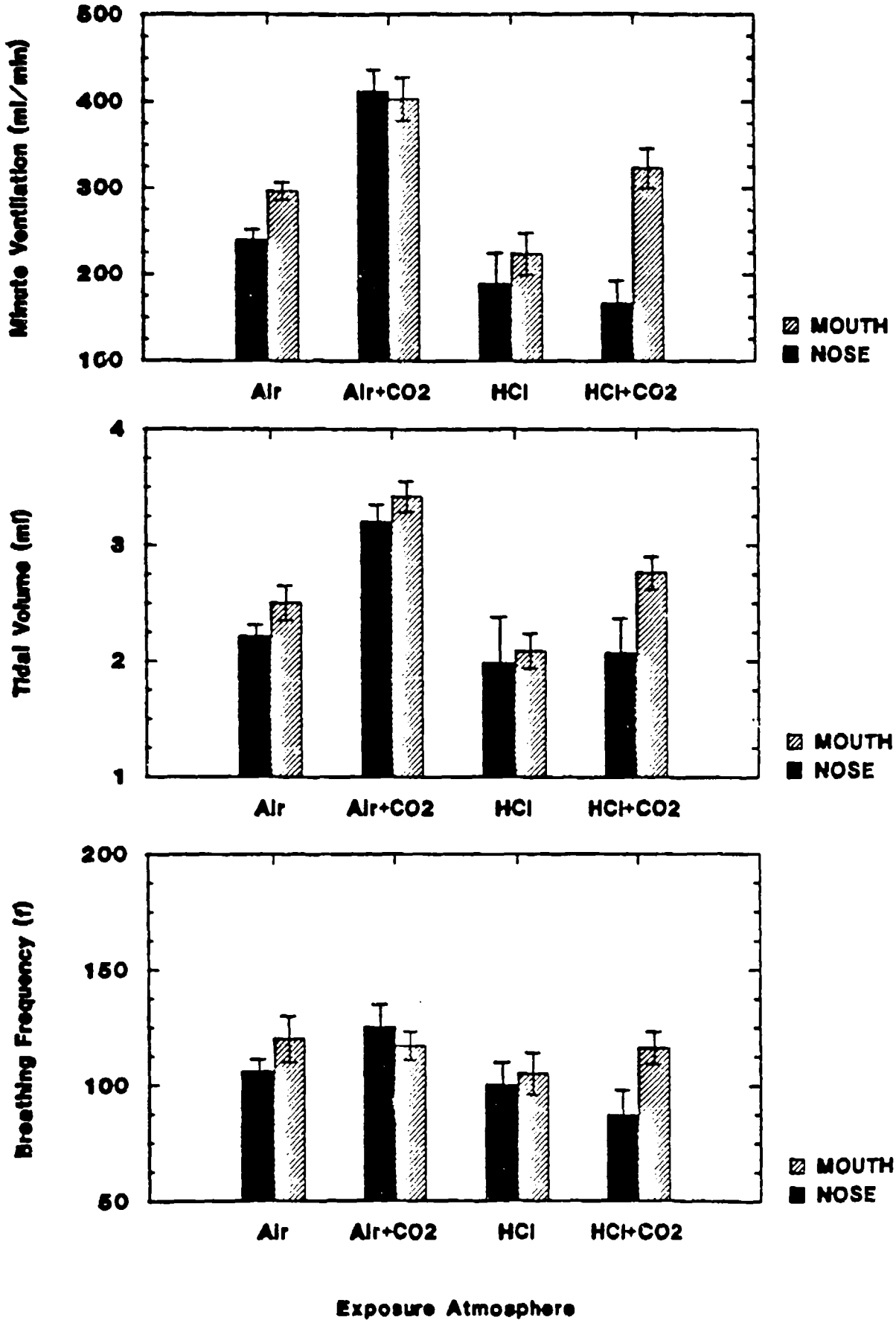


Figure 4. Minute ventilations, tidal volumes and breathing frequencies of rats exposed to air, air + 5% CO_2, 1000 ppm HCl or 1000 ppm HCl + 5% CO_2 via the nose or mouth. Values represent the mean and S.E.M. of n=6 to 12 rats.

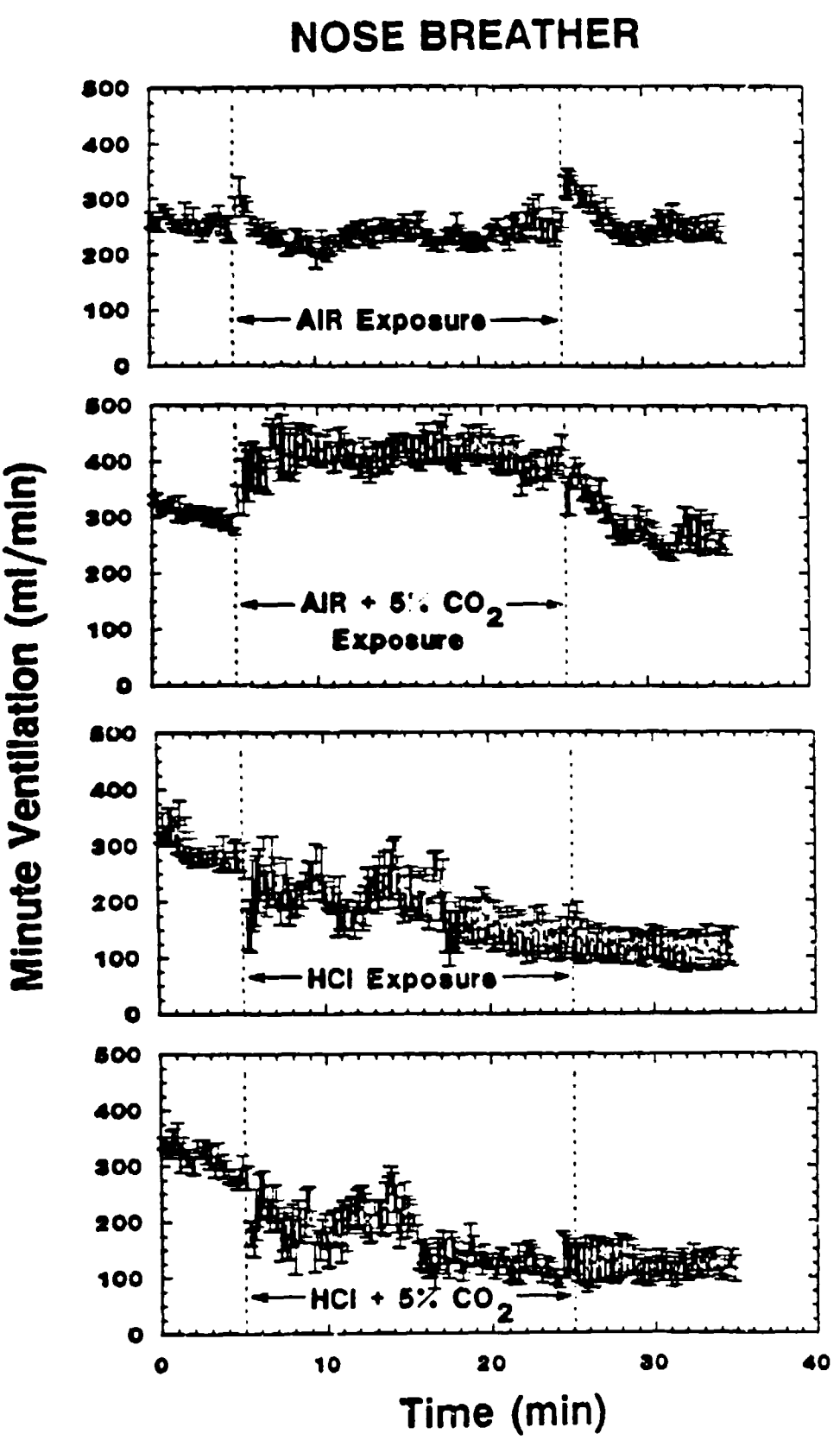


Figure 5. Minute ventilations of nose breathing (NB) rats before, during, and after exposure to air, air + 5% CO_2, 1000 ppm HCl, or 1000 ppm HCl + 5% CO_2. Each point represents the mean and standard error of the mean of average minute ventilation values for a 10 second period of time for n = 6 rats.

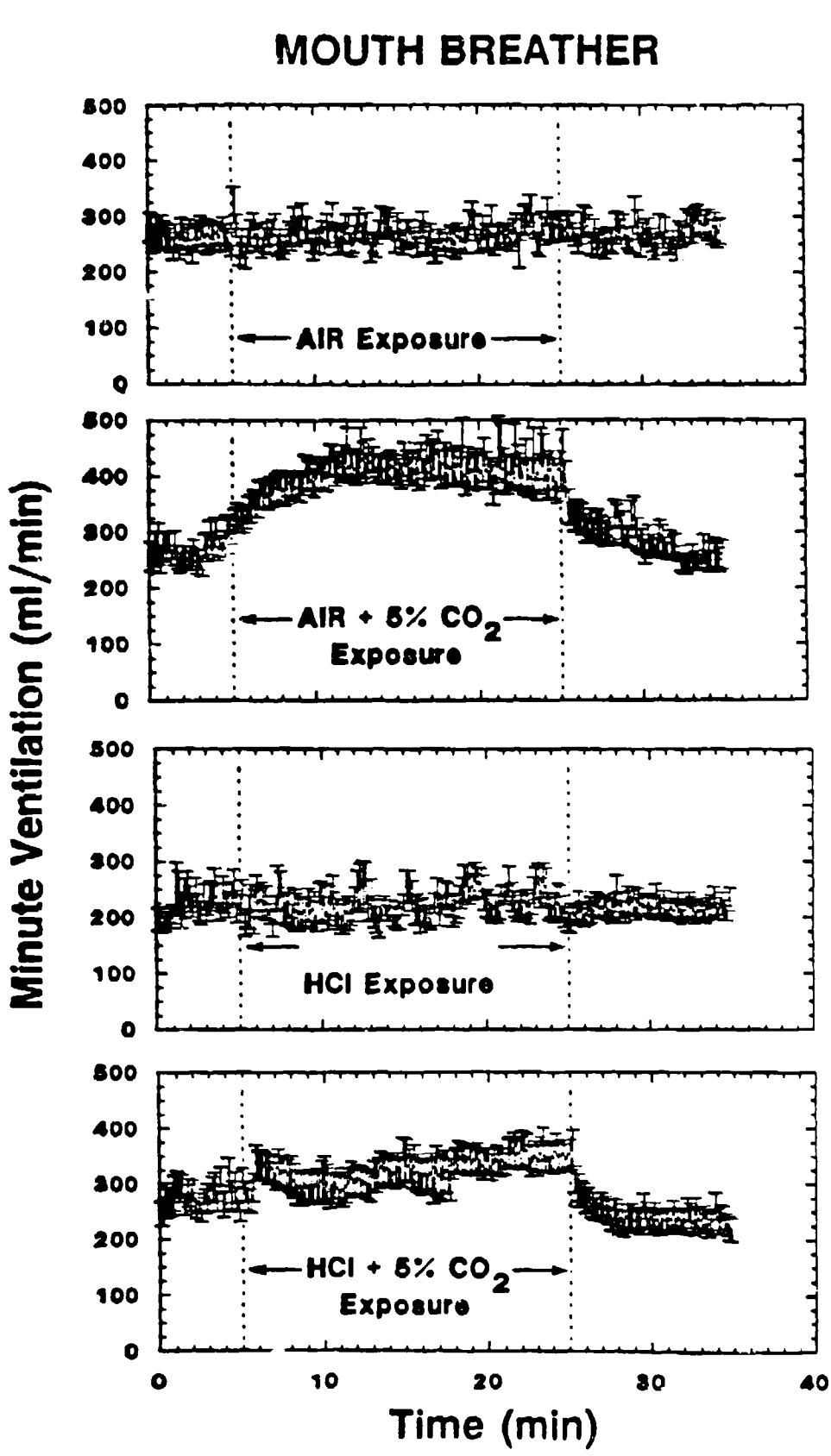


Figure 6. Minute ventilations of mouth breathing (MB) rats before, during, and after exposure to air, air + 5% CO_2, 1000 ppm HCl, or 1000 ppm HCl + 5% CO_2. Each point represents the mean and standard error of the mean of average minute ventilation values for a 10 second period of time for n = 6 to 12 rats.

CO_2 exposure of NB and MB animals were primarily the result of tidal volume (VT) changes, Figure 4. While breathing frequency (f) increased during air + CO_2 inhalation in the NB rats, no significant changes in f were measured in the MB rats. Elevation of VE measured in MB rats during HCl +CO_2 exposure were primarily due to increases in VT.

No post-exposure mortality was observed in NB animals after exposure to air, air + 5% CO_2, 1000 ppm HCl, or to 1000 ppm HCl + 5% CO_2 atmospheres. No post-exposure deaths occurred after MB rats were exposed to air, or air + 5% CO_2. However, MB rats experienced 40% mortality after exposure to 1000 ppm HCl and 58% mortality after exposure to 1000 ppm HCl + 5% CO_2. Compared to air exposed controls, NB animals exposed to HCl experienced significant body weight losses (~10% body weight reductions) as of 24 hrs. after exposure, Figure 7. HCl + 5% CO_2, which did not increase VE as noted above, caused no greater body weight reductions compared to the reductions observed after HCl-only exposures. MB animals in all groups, including air controls, experienced 24 hr body weight reductions, Figure 7. Compared to air exposed MB animals, the HCl exposed animals experienced significantly greater reductions in body weight. The addition of CO_2 with the HCl exposure, which increased VE as previously indicated, did not affect the body weight loss experienced 24 hrs. after exposure relativeto rats exposed to HCl only.

No significant differences were found in the lung wet weights (LWW) or right cranial lobe dry weights (RCLDW) of NB animals exposed to HCl or HCl + 5% CO_2 when compared to corresponding values obtained from the lungs of air exposed animals, Figures 8-9. The LWW, and RCLDW of MB animals exposed to HCl were not significantly different 24 hrs. after exposure compared to air exposed values, Figures 8-9. Significant increases in LWW and RCLDW, however, were measured from animals exposed to HCl + 5% CO_2 compared to values from animals exposed to HCl only.

Air or air + CO_2-exposed NB animals showed no abnormalities in the upper respiratory tract. Animals exposed to HCl had a moderate necrotizing rhinitis in Region I and sometimes Region II. The necrosis was multifocal with degeneration/regeneration (squamous epithelium) and accompanying exudates in the lumen. The lesion produced upon inhalation of HCl + CO_2 was not discernably different from the lesion in animals exposed to HCl alone. With the MB rats, the nasal sections were basically normal after inhalation of air, HCl, or these atmospheres with CO_2. Exudates or blood was occasionally found in the turbinates, especially in Regions III and IV. Region I sometimes had soft tissue changes in the hard palate mucosa/submucosa and on the outside of the nares.

No lesions occurred within the tracheae of NB rats after exposure to

Post Exposure Body Weight Loss

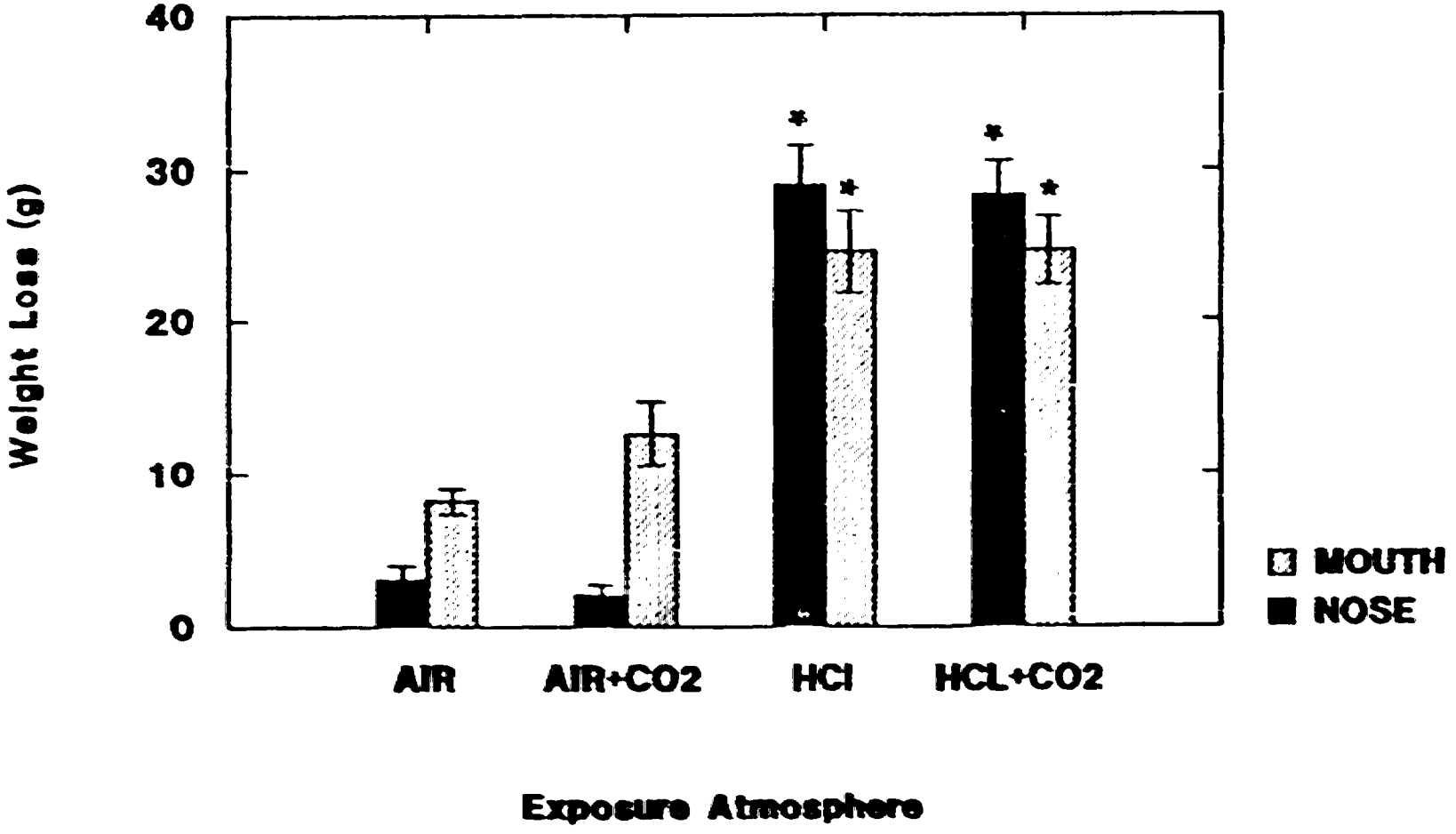


Figure 7. Body weight reductions of rats 24 hr after exposure via the mouth or nose to either air, air + 5% CO_2, 1000 ppm HCl or 1000 ppm HCl + 5% CO_2 for a period of 20 min. Values represent means and standard error of the mean of N = 5 to 6 rats. (*) indicate significant difference compared to body weight reductions found with rats exposed to air via the nose or mouth, $P \leq 0.05$.

Post Exposure Lung Wet Weight

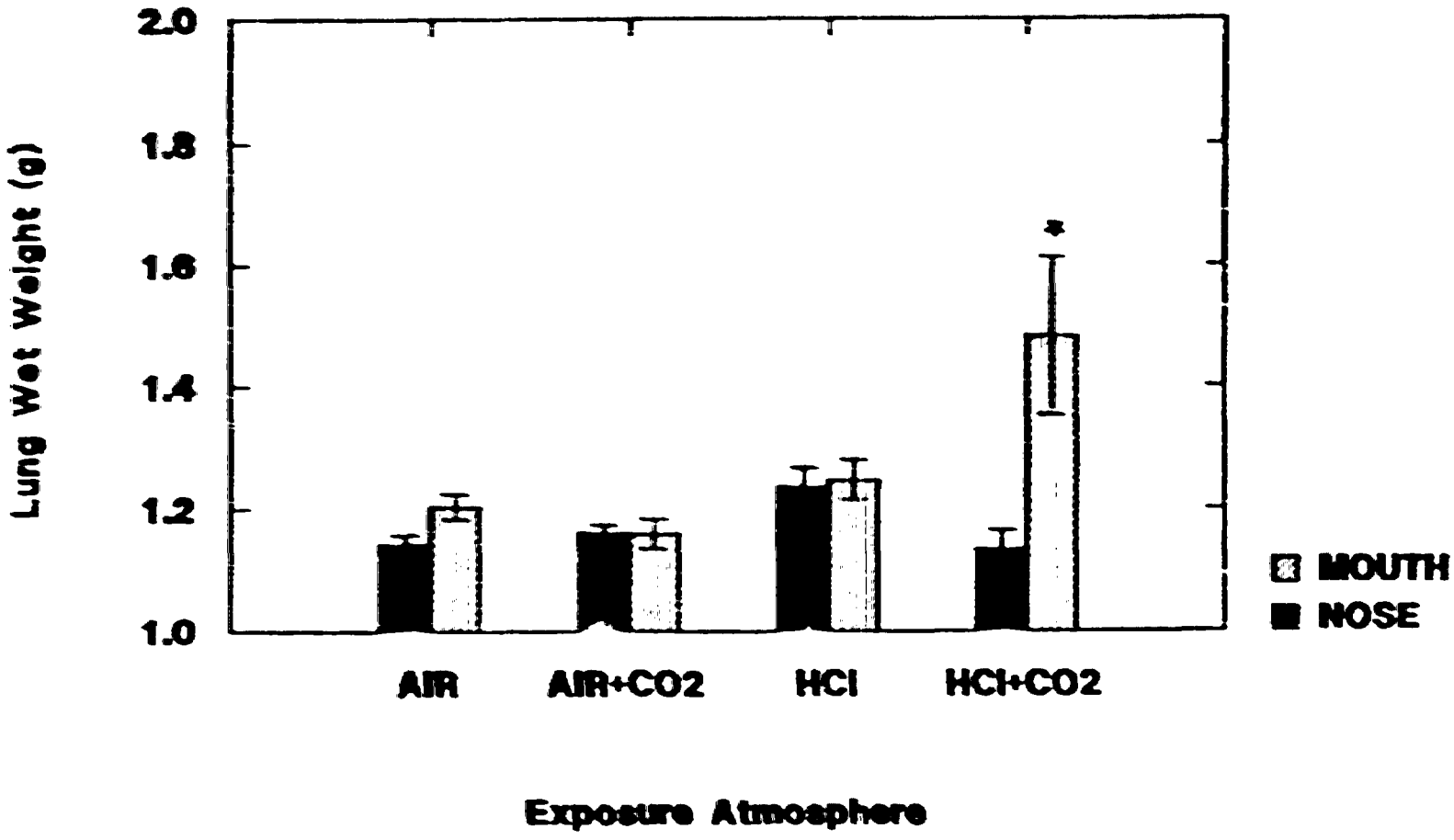


Figure 8. Lung wet weights (LWW) of rats 24 hr after exposure via the mouth or nose to either air, air + 5% CO_2, 1000 ppm HCl, or 1000 ppm HCl + 5% CO_2 for 20 min. Values represent the mean and standard error of the mean of N = 5 to 6 animals. (*) indicate significant difference compared to LWW found with rats exposed to air or HCl only via the mouth, $P \leq 0.05$.

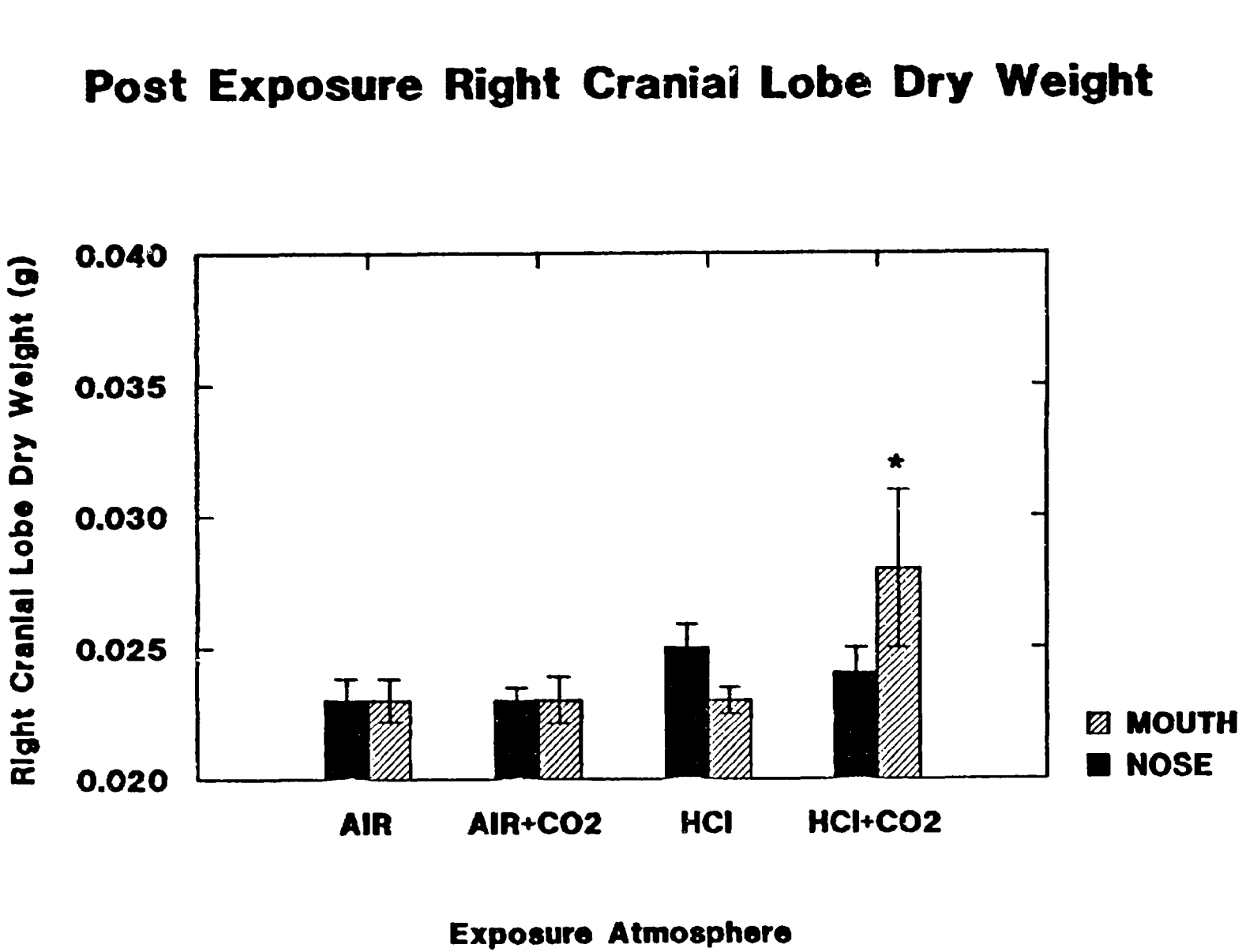


Figure 9. Right cranial lobe dry weight (RCLDW) of rats 24 hr after exposure via the mouth or nose to either air, air + 5% CO_2, 1000 ppm HCl, or 1000 ppm HCl + 5% CO_2 for 20 min. Values represent the mean and standard error of the mean of N = 5 to 6 animals. (*) indicate significant difference compared to RCLDW found with rats exposed to air or HCl only via the mouth. $P \leq 0.05$.

any of the experimental atmospheres. Air exposed MB rats showed a mild fibrino-suppurative tracheitis, mainly in the proximal trachea with neutrophils in the submucosa. MB rats exposed to HCl had a acute necrotizing tracheitis sometimes extending to the submucosa. PMN were observed in the submucosa and in tissues around the trachea with fibrinous pseudomembranes on the inner surface of the trachea. The tracheal injury of rats exposed to HCl + CO_2 was generally more severe, and it extended deeper into the lung. No lesions were found in the lower respiratory tract following NB exposure to air, air + CO_2, HCl, or HCl + CO_2. Air or air + CO_2 exposed MB animals showed no lesion in the lung compartment. The lungs from MB rats exposed to HCl alone were normal in appearance. The lungs of rats exposed to HCl + CO_2 showed necrosis of the major bronchus with PMN present in the submucosa. In the more peripheral conducting airways, there was minor necrosis of the bronchial or bronchiolar epithelium, but in some lungs there were large numbers of neutrophils in alveoli surrounding some terminal bronchioles. Edema fluid was observed in some rats. A summary of the pathologic lesion location is given in Table 1.

The results from this investigation can be summarized as follows:

• Inhalation of 5% CO_2 increased VE ~70% in NB animals and ~40% in MB animals. The increase in VE was primarily due to increases in VT in NB and MB animals.

• HCl inhalation during NB and MB decreased VE ~20%. NB animals did not increase VE during HCl + CO_2 inhalation, while MB animals increased VE ~45% during these exposures.

• The primary lesion resulting from NB inhalation of HCl was localized in the most anterior portion of the upper respiratory tract, and no additional injury was detected due to concurrent CO_2 inhalation.

• Inhalation of HCl during MB resulted in high mortality, which was increased with the elevated VE during concurrent CO_2 inhalation. Lung gravimetric and histologic parameters indicated that the surviving MB animals which were exposed to HCl + CO_2 developed more pronounced lower respiratory tract injury compared to MB animals exposed to HCl alone.

Halides and Deep Lung (Alveolar) Injury

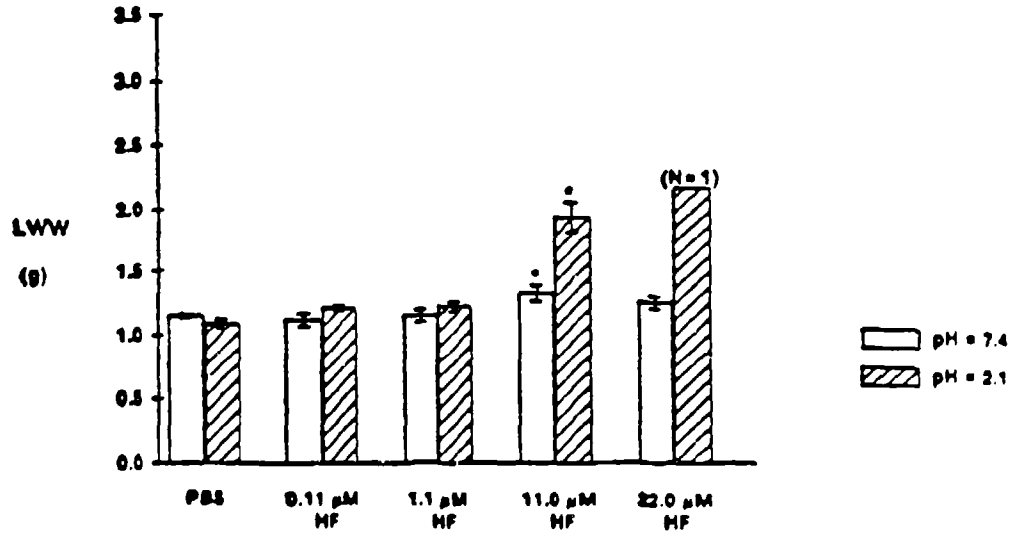
As previously indicated, the inhalation of the halides at relatively

PATHOLOGIC LESION LOCATION						
Exposure Atmosphere	Nasal Section I	Nasal Section II	Nasal Section III	Nasal Section IV	Trachea	Lung
NOSE BREATHER						
AIR						
AIR + CO_2						
HCl	++	+				
HCl + CO_2	++	+				
MOUTH BREATHER						
AIR					+	
AIR + CO_2					+	
HCl					++	
HCl + CO_2					+++	++

Table I. Pathologic lesion location 24 hr after acute inhalation of AIR, AIR + CO_2, HCl, HCl + CO_2. (+) indicates mild lesion, (++) indicates relatively moderate lesion, and (+++) indicates severe lesion.

high mass concentrations do not result in detectable injury in the lung's alveolar region. Various lines of evidence suggest that this may be due to an efficient deposition of the halides from the inhaled air stream prior to the entry of the inhaled air into alveolated structures. The possibility, however, has not been ruled out that the alveolar region may be less sensitive to the injurious effects of the halides, which in turn would suggest the existence of a local protective mechanism(s). In conjunction with a study we undertook for the Institute of Chemical Defense, we examined for the toxicity of HF when administered directly into the rat's lung via the intratracheal instillation of different doses of hydrofluoric acid in buffered saline. In addition, we compared the pulmonary injury produced by hydrofluoric acid in acid buffered saline (where the hydrofluoric acid is present primarily as HF) with that in neutral buffered saline (where the hydrofluoric acid is present primarily as F^-) when given by intratracheal instillation. Because the pK_a for hydrofluoric acid ic 3.19, we selected conditions of pH=2.1 in phosphate buffered saline (PBS) to give >90% HF ($[HF]/[F^-] = K_a/[H^+]$), and pH=7.4 to give >99% F^- ($[F^-]/[HF] = [H^+]/K_a$). The hydrofluoric acid in PBS was delivered to the lungs of rats by instillation of 0.5 ml of 0.22 mM, 2.2 mM, 22 mM and 44 mM hydrofluoric acid solutions resulting in dose quantities of 0.11 μM, 1.1 μM, 11 μM and 22 μM, respectively. Instillations of PBS, pH=7.4 and PBS, pH=2.1, were also included as controls. Lung wet weights (LWW) and right cranial lobe dry weights (RCLDW) were determined 24 hr after exposure, see Figure 10.

No significant increases in LWW or RCLDW were observed for rats exposed to either acidic PBS (pH 2.1), neutral PBS (pH 7.4), or for rats exposed to 0.11 μM, and 1.1 μM hydrofluoric acid in either acidic or neutral PBS, Figure 10. An ~7% increase in LWW observed for 11 μM hydrofluoric delivered in neutral (pH 7.4) PBS was significant at the p=0.05 level. However, based on the absence of any significant increase in LWW for 22 μM hydrofluoric acid in neutral PBS or increases in RCLDW for 11 μM and 22 μM hydrofluoric acid in neutral PBS, the statistical significance estimated for 11 μM hydrofluoric acid in neutral PBS was likely a type I error. Significant increases in LWW and RCLDW were observed for rats receiving 11 μM and 22 μM doses in acid-buffered (pH 2.1) PBS. In the group of 3 rats exposed to 22 μM HF in acid-buffered PBS, the instillation of one rat was unsuccessful, and one rat died within 12 hrs. after exposure; consequently, we obtained gravimetric data for only one rat at this dose. Because hydrofluoric acid is a weak acid in aqueous solution, the hydrofluoric acid in acid-buffered PBS exists primarily in the undissociated form HF; in neutral-buffered PBS, the hydrofluoric acid exists primarily as F^-. This fact and the lung gravimetric data



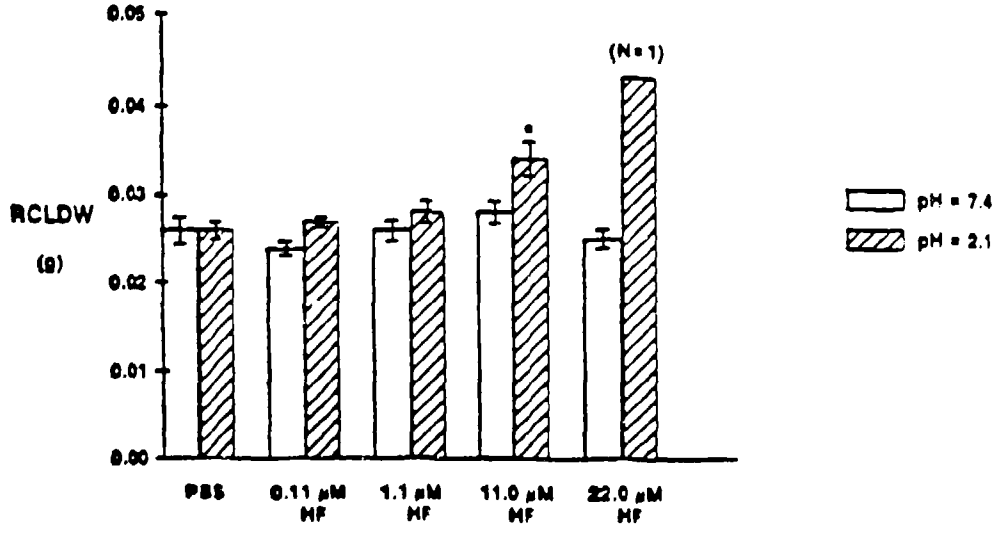


Figure 10: Lung wt weight (LWW) and right cranial lobe dry weight (RCLDW) 24 hours after exposure. * = significantly higher than PBS instilled controls, $p \leq 0.05$.

demonstrated that at 11 and 22 μM doses given by instillation, HF produces more lung injury than F^-. That neither neutral PBS or acidic PBS alone produced significant injury showed that neither the instillation procedure or the delivery of acid (H^+) in PBS results in significant tissue damage. Thus, the collective data argue for the involvement of HF rather than F^- or H^+ as the active species in pulmonary injury produced by hydrofluoric acid. Ultrastructural analyses of the lungs instilled with the toxic form of HF revealed marked damage to the alveolar epithelial surface. The above results, accordingly, indicate that HF can be toxic to the alveolar region. Thus, it appears that the lack of an injurious response to the halides in the alveolar region following their inhalation is due to their efficient removal from the inhaled air stream.

Particulate and Halide Gas Phase Effects

Numerous studies have demonstrate that the injurious effects of a variety of toxic gases are more pronounced when exposures occur concurrently with a particulate phase component, e.g., Last et al, Am. Rev Respir. Dis. 128:539-544, 1983; Last and Warren, Toxicol. Appl. Pharm. 90:34-42, 1987; Osebold et al, J. Environ. Path. Toxicol. 3:221-234, 1980; Nakamura, Jpn. J. Hyg. 10:322-333, 1964; Warren et al, Toxicol. Appl. Pharm. 84:470-479, 1986; Warheit et al, Exper. Mol. Path. 52:309-329, 1990; Holt and Keast, Bacteriol. Rev. 41:205-216, 1977; Koenig et al, Arch. Environ. Health 37:5-9, 1982; Gerde et al, Toxicol. Appl. Pharm. 108-1-13, 1991, Kulle et al, Environ. Res. 41:239-250, 1986; Schiff et al, Environ. Res. 19:339-354, 1979; Boren and Lake, Arch. Environ. Health 8:119-132, 1964. The mechanistic bases for such observations are potentially numerous. Under some conditions, at least, particles serve as carrier vehicles, which can enhance the deposition of adsorbed gases at sites in the respiratory tract where the particles preferentially deposit. In other instances, particulate materials that are generally considered to be relatively benign or noncytotoxic can cause an injurious response in addition to that caused by the inhaled gas when the particles fall within the ultra-fine range.

During FY 91, we undertook the development of aerosol technology in our laboratory (in collaboration with the University of Rochester) so that issues concerning the toxicity of atmospheres containing toxic gases and particles can be investigated. As indicated in the FY 92 Statement of Work, the initial specific objective of this effort is to determine how the profile and severity of injury to the respiratory tract following halide exposure may be altered by the concurrent inhalation of aerosolized particles.

Our first study was mainly undertaken to test our ability to generate

and deliver exposure atmospheres consisting of halide gas and aerosolized particles to rats. Three exposure groups of Fischer-344 rats (SPF) were used in this study, (N=6/group). Exposures were conducted while the animals (normal nose breathers) were positioned in whole body exposure tubes. Twenty min exposures were conducted with exposure atmospheres consisting of either 1000 ppm HCl, carbon particles (~0.8 μm geo. diam.), or 1000 ppm HCl + carbon particles. After cessation of the exposures, the animals were returned to their cages for a 24 hrs period prior to sacrifice. HCl only exposure atmospheres were generated by mixing pure HCl, (Matheson Gas, LaPorte, TX) with anhydrous HEPA filtered air in a quartz-glass mixing chamber and inhalation chamber. Exposure concentrations of HCl were determined by quantitatively drawing samples of the atmospheres through midget impingers. Ionic strength adjusting buffer, (ISA) was used as collection medium in the impingers, and it was analyzed with with calibrated, ion specific electrode, (Orion Research Inc. Cambridge, MA). A minimum of 3 discreet samples was measured for every 20 min exposure. The mean HCl concentration for the HCl only exposures was 1016 ± 21 ppm. Particulate carbon only atmospheres were generated via a aerosol generator (Jet-O-Miser Model 00, Fluid Energy Processing and Equipment Co., Hatfield, PA), which was fed carbon fines from a powder feeder (Accurate Model 102 Feeder, Accurate, Whitewater, WI). Exposure atmosphere particulate mass concentration was determined by filter analyses. Exposure atmospheres were combined using the same methodology described above for the rat group that received the carbon particles + HCl atmosphere. The mass concentration of carbon was ~178 mg/M^3, but some variation occurred during the actual exposures. Endpoints examined in this study were lung gravimetric changes and histopathologic changes in the lungs. The lung wet weights after exposure to HCl only, particulate carbon only, and HCl + particulate carbon were 1.179 ± 0.031 g, 1.20 g ± 0.027 g, and 1.20 ± 0.023 g, respectively. Right cranial lobe dry weights for these groups were 0.023 ± 0.0007 g, 0.024 ± 0.0004 g, and 1.20 ± 0.0013 g, respectively. Light microscopic assessments of the lungs from the animals in each group revealed no significant differences. The lack of a demonstrable effect due to the co-inhalation of particles and HCl may have been due to many variables. 1) We did experience some variability in maintaining a stable mass concentration of the particles during the exposures. 2) the mass concentration of particles, which was below that expected to occur in a real fire scenario, may have been too low. 3) the aerodynamic size distribution of the particles may not have been optimal to favor alveolar deposition. 4) the breathing patterns of the animals may have differed with the various exposure atmospheres.

Recent Reports

Lehnert, B.E., Stavert, D.M.: Pulmonary pathophysiology of oxides of nitrogen, and pulmonary pathophysiology of halide gases. Military Medical Pulmonary Research Review and Analysis, Ft. Fitzsimmons, Denver, CO, September 20-22, 1988.

Kusewitt, D.F., Stavert, D.M., Ripple, G., Mundie, T., Lehnert, B.E.: Relative acute toxicities in the respiratory tract of inhaled hydrogen fluoride, hydrogen bromide, and hydrogen chloride. 28th Annual Meeting of the Society of Toxicology. Atlanta, Ga, February 27-March 3, 1989. The Toxicologist 9:A144, 1989.

Archuleta, D., Stavert, D.M., Lehnert, B.E.: Pathologic responses to HF, HBr, or HCl inhaled by pseudo-mouth breathing and nose breathing rats. 29th Annual Meeting of the Society of Toxicology, Miami Beach, FL., February 12-16, 1990. The Toxicologist 10:A818, 1990.

Stavert, D.M., Archuleta, D., Behr, M.J., Lehnert, B.E.: Relative acute toxicities of hydrogen fluoride, hydrogen chloride and hydrogen bromide in nose- and pseudo-mouth-breathing rats. Fund. Appl. Toxicol. 16:636-655, 1991.

Archuleta, D., Martinez, M., Stavert, D.M., Lehnert, B.E.: Pathologic responses to inhaled HCl during periods of increased minute ventilation in pseudo-mouth breathing and nose breathing rats. 1991 Society of Toxicology Annual Meeting, Dallas TX, February 25-March 1, 1991. The Toxicologist 11(1): A339, 1991.

Lehnert, B.E., Kinkead, S.A., Kress, J.D., Kober, E.M., G.O. Wood, Stavert, D.M., Brainard, J.R.: Mechanism(s) of Lung Injury Caused by Perfluoroisobutylene (PFIB) and Related Agents. In: *Proceedings of the 1991 Medical Defense Biosciences Review.* pp. 273-291, 1991.

Brainard, J.R., Kinkead, S.A., Kober, E.M., Stavert, D.M., Lehnert, B.E.: Potential involvement of HF in mechanisms of pulmonary toxicity of perfluoroisobutylene. In: *Proceedings of the 1990 Scientific Conference on Chemical Defense Research* (in press), 1991.

Brainard, J.R., Kinkead, S.A., Wood, G.O., Stavert, D.M., Lehnert, B.E.: Potential involvement of hydrofluoric acid in perfluoroisobutylene-induced lung injury. 1992 Annual Meeting of the Society of Toxicology, Seattle, WA, February 23-27, 1992.

Oberdorster, G., Ferin, J., Finkelstein, J., Baggs, R., Stavert, D.M., Lehnert, B.E.: Health hazards from thermal degradation events: Particulate vs. gas phase effects. Intern. Conference on Environmental Systems, Aerospace Medical Association, Seattle, WA, July, 1992.